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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/811,143	03/15/2001	Lisa Kajisa	2719.2018-001	5798

7590 05/31/2002

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EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1637	5

DATE MAILED: 05/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/811,143	Applicant(s) KAJISA ET AL.	
	Examiner Jeffrey Fredman	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement filed June 25, 2001, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

While the IDS indicates that a copy of the references were filed, no references were found with the case.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Torrence et al (U.S. Patent 5,677,289).

Torrence teaches a method of preparing a nucleic acid on a solid support (column 11, line lines 34-45) comprising:

a) attaching a plurality of nucleic acids to the support to form an array (column 11, lines 34-42), (It is noted that the claim does not require the nucleic acids to be different from one another, nor spaced in any particular manner, so the antisense

molecules synthesized on the ABI 391 as taught by Torrence represent a plurality of identical nucleic acids attached to a support which form an array),

b) drying said array by exposing to a dry atmosphere for a period of at least 30 seconds (See column 11, lines 42-44 where Torrence dries the oligonucleotide for 60 seconds with anhydrous argon).

Torrence teaches synthesis of an oligonucleotide in the range of 5 to 50 nucleotides (see figure 8) where the drying follows a portion of the cycles, here the final cycle, with a drying time of at least 50 seconds, here 60 seconds (column 11, lines 34-45).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Torrence as applied to claims 1 and 2 above, further in view of Synthesis cycle 10hpaf3 (ABI 380B manual, Nov. 1989) and further in view of Yeung et al (Anal. Biochem. (1990) 18:66-75).

Torrence teaches a method of preparing a nucleic acid on a solid support (column 11, line lines 34-45) comprising:

a) attaching a plurality of nucleic acids to the support to form an array (column 11, lines 34-42), (It is noted that the claim does not require the nucleic acids to be different from one another, nor spaced in any particular manner, so the antisense molecules synthesized on the ABI 391 as taught by Torrence represent a plurality of identical nucleic acids attached to a support which form an array),

b) drying said array by exposing to a dry atmosphere for a period of at least 30 seconds (See column 11, lines 42-44 where Torrence dries the oligonucleotide for 60 seconds with anhydrous argon).

Torrence teaches synthesis of an oligonucleotide in the range of 5 to 50 nucleotides (see figure 8) where the drying follows a portion of the cycles, here the final cycle, with a drying time of at least 50 seconds, here 60 seconds (column 11, lines 34-45).

Torrence does not teach synthesis where every cycle is flushed with argon for an extended period of time.

The ABI Manual, synthesis cycle 10hpaf3, teaches a cycle in which argon flushing occurs repeatedly in 100% of the cycle coupling steps (where the reverse flush

shown in step numbers 18, 24, 26, 31, 50, 52 and 55 each represent a drying of the support using argon as the flushing agent) Further, the examiner notes that there is an additional 2.5 second delay inherent in the operation of the ABI 380B apparatus, yielding a complete drying time during the cycle of 35 seconds for any one step, and a combined drying time of 185 seconds for the 7 steps listed.

Yeung also demonstrates, in table I, the use of a reverse flush with argon in an ABI 380A synthesizer for 60 seconds at step 101 (page 67).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to dry the support using the cycle functions disclosed by the ABI manual in the method of Torrence for oligonucleotide synthesis in order to follow a standard, well designed protocol identified by the company as functional and because increased drying times would improve removal of unwanted components and improve quality of synthesis of the oligonucleotides. Specifically, an ordinary practitioner would recognize that the selection of specific flushing times for argon represents a balance between speed of the cycle versus quality of the resultant product. Increased time would be expected to slow the cycle time down but would also be expected to increase the quality of the product by removing products, such as the capping components, which can damage the nucleic acids being synthesized. Yeung provides evidence that optimization of these elements was routine in the art, as Yeung notes "We formulated the FC3 program and a procedure by which a DNA synthesizer designer or operator can use 18-base-long homopolymers of A, G, C, and T to optimize the reaction times, reagent concentrations, solvent wash conditions and the many steps

in the synthesis cycle (abstract)". This optimization further supports the obviousness of the claim given that Yeung's optimized protocol, designed to minimize reagent use, still uses an argon drying step of over 60 seconds (see table I).

7. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Torrence as applied to claims 1 and 2 above, further in view of Synthesis cycle 10hpaf3 (ABI 380B manual, Nov. 1989) and further in view of Yeung et al (Anal. Biochem. (1990) 18:66-75). And further in view of McGall et al (U.S. Patent 6,147,205).

Torrence in view of Synthesis cycle and further in view of Yeung teach the limitations of claims 1-5 as discussed above.

Torrence in view of Synthesis cycle and further in view of Yeung do not teach the masking and photoremovable synthesis method nor do they teach 100,000 different nucleic acid sequences being synthesized in a region less than 1 square millimeter.

McGall teaches a method of nucleic acid synthesis using photoremovable synthesis and masking (column 2, line 57 to column 3, line 19) comprising

(a) activating a region of the support (column 2, line 58)

(b) binding a molecule to the region, said molecule comprising a masked reactive site linked to a photolabile protecting group such as a labeled nucleotide (column 2, line 59 to column 3, line 2 and column 6, line 62 to column 8, line 19)

(c) repeating steps (a) and (b) on other regions of the support whereby each of said other regions has bound thereto another molecule comprising a masked reactive site linked to the photolabile protecting group, wherein said another molecule may be the same or different from that used in step (b) (column 3, lines 3-8);

(d) removing the photolabile protecting group from one of the molecules bound to one of the regions of the support to provide a region bearing a molecule with an unmasked reactive site (column 3, lines 9-12)

(e) binding an additional molecule to the molecule with an unmasked reactive site (column 3, lines 13-14),

(f) repeating steps (d) and (e) on regions of the support until a desired plurality of compounds is formed from the component molecules, each compound occupying separate regions of the support (column 3, lines 15-29).

McGall expressly teaches the use of masks (column 18, line 7) as well as expressly teaching multiple reactants simultaneously applied (column 10).

McGall further teaches that the region can be small than 1 square millimeter (column 5, line 32) as well as that arrays may include 10^6 or more different polymers (see column 13, lines 18-26).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to synthesize arrays using the method of McGall combined with the optimized washing conditions of 30 to 185 seconds provided by Torrence, ABI synthesis cycle 10hpaf3 and Yeung since an ordinary practitioner would have been motivated to optimize the method of McGall to minimize the interfering effects of mixed components upon the synthesis reaction and since as Yeung notes "We formulated the FC3 program and a procedure by which a DNA synthesizer designer or operator can use 18-base-long homopolymers of A, G, C, and T to optimize the reaction times, reagent concentrations, solvent wash conditions and the many steps

in the synthesis cycle (abstract)". This optimization further supports the obviousness of the claim given that Yeung's optimized protocol, designed to minimize reagent use, still uses an argon drying step of over 60 seconds (see table I).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

May 23, 2002